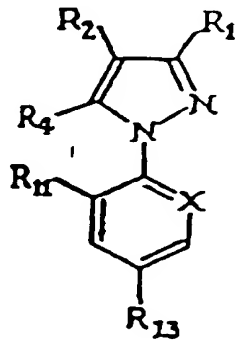
CLAIMS

1. Composition for long-lasting protection against fleas on small mammals, and in particular cats and dogs, characterized in that it includes, on the one hand, at least one compound (A) belonging to the formula (I),



(I)

in which:

R_1 is CN or methyl or a halogen atom;

R_2 is $S(O)_nR_3$ or 4,5-dicyanoimidazol-2-yl or haloalkyl;

R_3 is alkyl or haloalkyl;

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6, $S(O)_mR_7$, $C(O)R_7$, $C(O)O-R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)(R_{10})$;

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, C(O)alkyl, alkoxycarbonyl or $S(O)_r-CF_3$ radical; R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms such as oxygen or sulphur;

R_7 represents an alkyl or haloalkyl radical;

R_8 represents an alkyl or haloalkyl radical or a hydrogen atom;

R_9 represents an alkyl radical or a hydrogen atom;

R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, S-alkyl, cyano or alkyl;

R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom, or optionally CN or NO_2

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $S(O)_qCF_3$ or SF_5 group;

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2;

X represents a trivalent nitrogen atom or a radical $C\text{-}R_{12}$, the other three valency positions of the carbon atom forming part of the aromatic ring;

with the proviso that when R_1 is methyl, then R_3 is haloalkyl, R_4 is NH_2, R_{11} is Cl, R_{13} is CF_3 and X is N; or R_2 is 4,5-dicyanoimidazol-2-yl, R_4 is Cl, R_{11} is Cl, R_{13} is CF_3 and X is =C-Cl;

and, on the other hand, at least one ovicidal compound (B), of insect growth regulator (IGR) type, in a fluid vehicle which is acceptable to the animal and suitable for local application on the skin.

2. Composition according to claim 1, characterized in that the compound of formula (I) is such that:

R_1 is CN or methyl

R_2 is $S(O)_nR_3$

R_3 is alkyl or haloalkyl

R_4 represents a hydrogen or halogen atom; or a radical NR_5R_6, $S(O)_mR_7$, $C(O)R_7$, alkyl, haloalkyl or OR_8 or a radical $-N=C(R_9)\ (R_{10})$

R_5 and R_6 independently represent a hydrogen atom or an alkyl, haloalkyl, C(O)alkyl or $S(O)_r\text{-}CF_3$ radical; or R_5 and R_6 may together form a divalent alkylene radical which may be interrupted by one or two divalent hetero atoms such as oxygen or sulphur

R_7 represents an alkyl or haloalkyl radical

R_8 represents an alkyl or haloalkyl radical or a hydrogen atom

R_9 represents an alkyl radical or a hydrogen atom

R_{10} represents a phenyl or heteroaryl group optionally substituted with one or more halogen atoms or groups such as OH, -O-alkyl, S-alkyl, cyano or alkyl

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R_{11} and R_{12} represent, independently of each other, a hydrogen or halogen atom

R_{13} represents a halogen atom or a haloalkyl, haloalkoxy, $S(O)_qCF_3$ or SF_5 group

m, n, q and r represent, independently of each other, an integer equal to 0, 1 or 2

X represents a trivalent nitrogen atom or a radical C-R_{12}, the other three valency positions of the carbon atom forming part of the aromatic ring

with the proviso that when R_1 is methyl, then R_3 is haloalkyl, R_4 is NH_2, R_{11} is Cl, R_{13} is CF_3 and X is N.

3. Composition according to claim 1, characterized in that the compound of formula (I) is such that R_1 is CN.

4. Composition according to claim 1, characterized in that the compound of formula (I) is such that R_{13} is haloalkyl, preferably CF_3.

5. Composition according to claim 1, characterized in that the compound of formula (I) is such that R_2 is $S(O)_nR_3$, preferably with n = 1, R_3 preferably being CF_3 or alkyl, in particular methyl or ethyl, or n = 0, R_3 preferably being CF_3.

6. Composition according to claim 1, characterized in that the compound of formula (I) is such that X is C-R_{12} with R_{12} being a halogen atom.

7. Composition according to claim 1, in which the compound of formula (I) is such that R_1 is CN, R_3 is haloalkyl, R_4 is NH_2, R_{11} and R_{12} are, independently of each other, a halogen atom, and/or R_{13} is haloalkyl.

8. Composition according to claim 1, in which the compound of formula (I) is:
1-[2,6-Cl_2 4-CF_3 phenyl] 3-CN 4-[SO-CF_3]5-NH_2 pyrazole, commonly known as Fipronil

9. Composition according to claim 1, in which the compound of formula (I) is one of the following compounds:

1: 1-[2,6-Cl_2 4-CF_3 phenyl] 3-CN 4-[S-CF_3]5-NH_2 pyrazole, commonly known as Fipronil

2: 1-[2,6-Cl_2 4-CF_3 phenyl] 3-CN 4-[SO-C_2H_5]5-NH_2 pyrazole

10. Composition according to claim 1, characterized in that the compound (B) is a compound which mimics juvenile hormones, in particular:

azadirachtin
diofenolan
fenoxycarb
hydroprene
kinoprene
methoprene
pyriproxyfen
tetrahydroazadirachtin

and 4-chloro-2-(2-chloro-2-methyl-propyl)-5-(6-iodo-3-pyridylmethoxy)pyridizine-3(2H)-one or a chitin-synthesis inhibitor, in particular:

chlorfluazuron
cyromazine
diflubenzuron
fluazuron
flucycloxuron
flufenoxuron
hexaflumuron
lufenuron
tebufenozide
teflubenzuron
triflumuron

1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(trifluoromethyl)phenylurea, 1-(2,6-difluoro-benzoyl)-3-(2-fluoro-4-(1,1,2,2-tetrafluoroethoxy)-phenylurea and 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-trifluoro-methyl)phenylurea.

~~11.~~ Composition according to claim ~~1,~~ characterized in that compound (B) is novaluron.

~~12.~~ Composition according to claim ~~10,~~ characterized in that the compound of IGR type is chosen from methoprenes, pyriproxyfens, lufenuron, hydroprene, cryromazine and 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(trifluoromethyl)phenylurea.

13. Composition according to claim 1, characterized in that the proportions, by weight, of compounds (A) of formula (I) and of compounds of type (B) are between 80/20 and 20/80.

14. Composition according to claim 1, characterized in that the fluid vehicle and the concentration of the compounds (A) and (B) are adapted to point application by deposition of "spot-on" type to the skin.

15. Composition according to claim 1, characterized in that the fluid vehicle and the concentration of the compounds (A) and (B) are adapted to local application by deposition of "pour-on" type to the skin.

16. Composition according to claim 1, characterized in that the fluid vehicle and the concentration of the compounds (A) and (B) are adapted to local application on a zone with a surface area of less than 10 cm^2, especially between 5 and 10 cm^2, in particular at two points and preferably localized between the animal's shoulders.

17. Composition according to claim 1, characterized in that it contains a dose of from 0.1 to 40 mg/kg of compound (A) and from 0.1 to 40 mg/kg of compound (B).

18. Composition according to claim 17, characterized in that it contains a dose of from 1 to 20 mg/kg, in particular from 2 to 10 mg/kg, of compound (A) and from 1 to 30 mg/kg, in particular 2 to 20 mg/kg, of compound (B).

19. Composition according to claim 14, characterized in that it also comprises a crystallization inhibitor (b), which is present in particular in a proportion of from 1 to 20% (W/V), preferably from 5 to 15%.

20. Composition according to claim 19, characterized in that the crystallization inhibitor (b) is chosen from:

- polyvinylpyrrolidone, polyvinyl alcohols, copolymers of vinyl acetate and vinylpyrrolidone, polyethylene glycols, benzyl alcohol, mannitol, glycerol, sorbitol, polyoxyethylenated sorbitan esters; lecithin,

sodium carboxymethylcellulose, acrylic derivatives such as methacrylates and the like,

- anionic surfactants such as alkaline stearates, in particular sodium, potassium or ammonium stearate; calcium stearate; triethanolamine stearate; sodium abietate; alkyl sulphates, in particular sodium lauryl sulphate and sodium cetyl sulphate; sodium dodecylbenzenesulphonate, sodium dioctylsulphosuccinate; fatty acids, in particular those derived from coconut oil,

- cationic surfactants such as water-soluble quaternary ammonium salts of formula $N^+R'R"R'"R"",Y^-$ in which the radicals R are optionally hydroxylated hydrocarbon radicals and Y^- is an anion of a strong acid such as the halide, sulphate and sulphonate anions; cetyltrimethylammonium bromide is among the cationic surfactants which can be used,

- amine salts of formula $N^+R'R"R'"$ in which the radicals R are optionally hydroxylated hydrocarbon radicals; octadecylamine hydrochloride is among the cationic surfactants which can be used,

- nonionic surfactants such as optionally polyoxyethylenated sorbitan esters, in particular polysorbate 80, polyoxyethylenated alkyl ethers; polyethylene glycol stearate, polyoxyethylenated derivatives of castor oil, polyglycerol esters, polyoxyethylenated fatty alcohols, polyoxyethylenated fatty acids, copolymers of ethylene oxide and propylene oxide,

- amphoteric surfactants such as substituted lauryl compounds of betaine,

or preferably a mixture of at least two of these crystallization inhibitors.

21. Composition according to claim 19, characterized in that it comprises a crystallization inhibitor couple formed by the combination of a film-forming agent of polymeric type and a surfactant, in particular in similar or identical amounts within the

limit of the total amounts of crystallization inhibitor.

22. Composition according to claim 21, characterized in that the film-forming agent is chosen from:

- the various grades of polyvinylpyrrolidone,
- polyvinyl alcohols, and
- copolymers of vinyl acetate and vinyl pyrrolidone,

and in that the surfactant is chosen from non-ionic surfactants, preferably polyoxyethylenated sorbitan esters, in particular the various grades of polysorbate.

23. Composition according to claim 14, characterized in that it comprises an organic solvent (c) having a dielectric constant of between 10 and 35, preferably 20 and 30, whose content in the overall composition preferably represents the difference to 100% of the composition.

24. Composition according to claim 23, characterized in that the organic solvent (c) is chosen from acetone, acetonitrile, benzyl alcohol, butyldiglycol, dimethylacetamide, dimethylformamide, dipropylene glycol n-butyl ether, ethanol, isopropanol, methanol, ethylene glycol monoethyl ether, ethylene glycol monomethyl ether, monomethylacetamide, dipropylene glycol monomethyl ether, liquid polyoxyethylene glycols, propylene glycol, 2-pyrrolidone, in particular N-methylpyrrolidone, diethylene glycol monoethyl ether, ethylene glycol, diethyl phthalate, or a mixture of at least two of these solvents.

25. Composition according to claim 23, characterized in that it also comprises an organic co-solvent (d) having a boiling point below 100°C, preferably below 80°C, and having a dielectric constant of between 10 and 40, preferably between 20 and 30, which is miscible with water and/or with the solvent (c), this co-solvent being present in particular in a

co-solvent (d)/solvent (c) weight/weight (W/W) ratio of between 1/15 and 1/2.

26. Composition according to claim 25, characterized in that the co-solvent (d) is chosen from absolute ethanol, isopropanol and methanol.

27. Composition according to claim 1, characterized in that it is made in the form of a kit combining, separately, in the same packaging, at least one container containing a compound (A) and at least one container for compound (B), and a notice specifying that the containers are to be used alternately with an interval, in particular of one month.

28. Composition according to claim 1, characterized in that it affords protection for 2 to 3 months.

29. Composition according to claim 2, in which the compound of formula (I) is such that R_1 is CN, R_3 is haloalkyl, R_4 is NH_2, R_{11} and R_{12} are, independently of each other, a halogen atom, and/or R_{13} is haloalkyl.

30. Composition according to claim 29, wherein X is $C\text{-}R_{12}$.

31. Composition according to claim 2, in which the compound of formula (I) is:
1-[2,6-Cl_2 4-CF_3 phenyl] 3-CN 4-[SO-CF_3]5-NH_2 pyrazole.

32. Composition according to claim 2, characterized in that the compound (B) is a compound which mimics juvenile hormones, in particular:

azadirachtin
diofenolan
fenoxycarb
hydroprene
kinoprene
methoprene
pyriproxyfen
tetrahydroazadirachtin
and 4-chloro-2-(2-chloro-2-methyl-propyl)-5-(6-iodo-3-pyridylmethoxy)pyridizine-3(2H)-one

or a chitin-synthesis inhibitor, in particular:

chlorfluazuron
cyromazine

diflubenzuron
fluazuron
flucycloxuron
flufenoxuron
hexaflumuron
lufenuron
tebufenozide
teflubenzuron
triflumuron
1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(trifluoromethyl)phenylurea, 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(1,1,2,2-tetrafluoroethoxy)-phenylurea and 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-trifluoro-methyl)phenylurea.

33. Composition according to claim 32, characterized in that the compound of IGR type is chosen from methoprenes, pyriproxyfens, lufenuron, hydroprene, cryromazine and 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(trifluoromethyl)phenylurea.

34. Composition according to claim 2, characterized in that the proportions, by weight, of compounds (A) of formula (I) and of compounds of type (B) are between 80/20 and 20/80.

35. Composition according to claim 2, characterized in that the fluid vehicle and the concentration of the compounds (A) and (B) are adapted to point application by deposition of "spot-on" type to the skin.

36. Composition according to claim 2, characterized in that it contains a dose of from 0.1 to 40 mg/kg of compound (A) and from 0.1 to 40 mg/kg of compound (B).

37. Composition according to claim 36, characterized in that it contains a dose of from 1 to 20 mg/kg, in particular from 2 to 10 mg/kg, of compound (A) and from 1 to 30 mg/kg, in particular 2 to 20 mg/kg, of compound (B).

38. Process for controlling fleas on small mammals, and in particular cats and dogs, over a long period, characterized in that the animal is treated by local application to the skin of parasiticidally effective

doses and proportions of a composition according to claim 1.

39. Process according to claim 38, wherein the compound (B) is a compound which mimics juvenile hormones, in particular:

azadirachtin
diofenolan
fenoxycarb
hydroprene
kinoprene
methoprene
pyriproxyfen
tetrahydroazadirachtin
and 4-chloro-2-(2-chloro-2-methyl-propyl)-5-(6-iodo-3-pyridylmethoxy)pyridizine-3(2H)-one

or a chitin-synthesis inhibitor, in particular:

chlorfluazuron
cyromazine
diflubenzuron
fluazuron
flucycloxuron
flufenoxuron
hexaflumuron
lufenuron
tebufenozide
teflubenzuron
triflumuron
1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(trifluoromethyl)phenylurea, 1-(2,6-difluoro-benzoyl)-3-(2-fluoro-4-(1,1,2,2-tetrafluoroethoxy)-phenylurea and 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-trifluoro-methyl)phenylurea.

40. Process according to claim 39, wherein the compound of IGR type is chosen from methoprenes, pyriproxyfens, lufenuron, hydroprene, cryromazine and 1-(2,6-difluorobenzoyl)-3-(2-fluoro-4-(trifluoromethyl)phenylurea.

41. Process according to claim 38, wherein compound (B) is novaluron.

42. Process according to claim 38, wherein the proportions, by weight, of compounds (A) of formula (I) and of compounds of type (B) are between 80/20 and 20/80.

43. Process according to claim 38, characterized in that the animal is treated by local point application to the skin of "spot-on" type.

44. Process according to claim 38, wherein it contains a dose of from 0.1 to 40 mg/kg of compound (A) and from 0.1 to 40 mg/kg of compound (B).

45. Process according to claim 38, wherein it contains a dose of from 1 to 20 mg/kg, in particular from 2 to 10 mg/kg, of compound (A) and from 1 to 30 mg/kg, in particular 2 to 20 mg/kg, of compound (B).

46. ~~Process according to claim 38, wherein the~~ animal is ~~treated~~ by depositing on the skin, in parasitically effective doses and proportions, a composition according to claim 2.

47. Process according to claim 38, wherein the animal is treated by depositing on the skin, in parasitically effective doses and proportions, a ~~composition according to claim 8.~~

48. Process according to claim 38, for controlling ectoparasites~~, in particular ticks~~.